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REQUEST FOR PRE-APPEAL BRIEF PANEL REVIEW

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Attorney Docket No.	RICE-012
Confirmation No.	8868
First Named Inventor	DALY, ROGER JOHN
Application Number	09/509,196
Filing Date	March 23, 2000
Group Art Unit	1649
Examiner Name	CHERNYSHEV, OLGA N.
Title:	"A POTENTIAL EFFECTOR FOR THE GRB7 FAMILY OF SIGNALLING PROTEINS"

Sir:

Applicants request panel review of the final rejection in the above-identified application. No amendments are being filed with this request. This request is filed with a Notice of Appeal.

The review is requested for the reasons outlined on the accompanying sheets.

The undersigned are attorneys of record.

Respectfully submitted,

Date: April 28, 2006

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The Claims

The pending claims are drawn in pertinent part to an isolated polynucleotide molecule comprising a nucleotide sequence having at least 95% sequence identity to a nucleotide sequence encoding SEQ ID NO:2, as well as vectors, transformed host cells, and methods of producing a protein by culturing such transformed host cells. The claimed polynucleotides include: isolated polynucleotides comprising a sequence as shown in SEQ ID NO:1, nucleotides 694-1614 of SEQ ID NO:1, or comprising a sequence having at least 95% sequence identity to SEQ ID NO:1; isolated polynucleotides comprising a sequence encoding an amino acid sequence of SEQ ID NO:2, or amino acid residues 232-538 of SEQ ID NO:2; isolated polynucleotides comprising a sequence having at least 95% sequence identity to a sequence encoding amino acid residues 232-538 of SEQ ID NO:2; isolated polynucleotides comprising a sequence of nucleotides 694-1614 of SEQ ID NO:1; and isolated polynucleotides comprising a sequence encoding amino acid residues 232-888 of SEQ ID NO:2.

Rejection of Claims 5-7, 19-22, 24-29, and 31-41 under 35 U.S.C. § 101

Review of this rejection is requested.

In summary, the rejection is based on the Examiner's allegation that the claimed invention has no apparent or disclosed specific and substantial credible utility. Applicants submit that this rejection is flawed both legally and procedurally and should be withdrawn.

Legal Flaws in the Rejection

Applicants' specification discloses at least two utilities for the claimed invention:

1) The claimed polynucleotides are useful in distinguishing cancer cells from normal cells because they are differentially expressed in certain human cancers, e.g., breast and prostate cancer; and

2) The claimed polynucleotides are useful for distinguishing cancer cells from normal cells because they encode a polypeptide (designated 2.2412) that binds to the signaling proteins Grb7 and to Grb14, each of which is known to be differentially expressed in certain cancer cells relative to normal cells. Therefore, because the 2.2412 polypeptides act as "bait" for Grb7 and Grb14, it is useful in detection of a tumor marker and/or a prognostic indicator for these cancers.

With regard to the above utilities, Applicants have established in the file record that it was known in the art as of Applicants' filing date that Grb7 and Grb14 are differentially expressed in cancer

cells (breast, prostate, gastric, and esophageal cancer) compared to normal cells. Applicants have provided extrinsic evidence that Grb7 and Grb14 were recognized as markers for cancer at the time of filing of the present application, as well as extrinsic and intrinsic evidence[1] that the 2.2412 polypeptide encoded by the claimed polynucleotide specifically binds to Grb7 and Grb14.

The Examiner dismissed the above evidence by virtue of her position that there is no factual evidence within the instant disclosure regarding differential expression of the polynucleotide encoding 2.2412. She appears to be requiring data showing altered levels or forms of a polynucleotide encoding 2.2412 polypeptide in diseased tissue versus corresponding healthy tissue. She criticized some data published before Applicants' filing date regarding differential expression as "inconclusive." She dismissed other articles published before Applicants' filing date relating to coexpression and coamplification of Grb7 in gastric and esophageal cancers because Applicants' specification does not disclose these types of cancer. She apparently has not considered evidence published after the filing date that supports Applicants' statements of utility.

The Examiner also appears to be confusing a statement of utility, which must be recited in the application as filed, with extrinsic evidence that supports such a statement. The latter evidence in support of a utility statement need not appear in the application as filed. Applicants have cited *In re Hogan*, 194 USPQ 527, 537 (CCPA 1977), which held that later publications that substantiate Applicant's assertions of utility or other art-related facts existing on the filing date are acceptable. The Examiner acknowledged this citation in the Final Office Action, but her only response to this and to all of Applicants' other arguments was a discussion of *In re Fisher*, 421 F.3d 1365 (Fed. Cir. 2005). Applicants will discuss *Fisher* below.

Applicants have disclosed[2] that the Grb7 family proteins exhibit differential expression in certain human cancers (particularly breast and prostate cancer) (emphasis added). The phrase *certain human cancers* is a generic statement that embraces the gastric and esophageal cancers disclosed by the Kishi *et al.* and Tanaka *et al.* articles, respectively, cited by Applicants in support of their utility statement. Apparently the Examiner is requiring that a generic statement of utility be accompanied by an exhaustive litany of specific utilities that fall within the generic utility statement in order for earlier or

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[1] See the specification at, for example, pages 10-11.

[2] See the specification at, for example, page 5.

later published specific knowledge to substantiate Applicants' assertion of utility. This is an unduly burdensome and also an improper standard.

Applicants submit that the standard used by the Examiner for satisfying the utility requirement is higher than that set forth in the § 101 Guidelines or Training Materials. To satisfy the utility requirement an applicant need only provide one credible assertion of specific and substantial utility for each claimed invention. MPEP § 2107 II(B). Applicants have provided at least two assertions of utility in their specification (see above) that satisfy the utility requirement. If the asserted utility is credible and if it is *more likely than not* that a person of ordinary skill in the art would consider the asserted utility specific and substantial, the utility requirement is met. MPEP § 2107 II(C). This is a preponderance of the evidence standard, a relatively low standard, which is lower than a clear and convincing evidence standard, which itself is lower than a beyond a reasonable doubt standard.

In this regard, extrinsic evidence, especially published before Applicants' filing date, is also evidence of the level of skill in the art. Therefore, Applicants have properly relied upon such evidence to substantiate their utility statement. In addition, because of the evidentiary standard set forth in MPEP § 2107 II(C) (see above), such evidence should be considered by the Examiner in evaluating a utility statement as being credible or specific and substantial. However, the Examiner has dismissed the relevance of the cited extrinsic evidence because she appears to be confusing *insertion* of a utility statement after the filing date with substantiation of a *utility* statement by extrinsic evidence (see above).

Moreover, by requiring data, the Examiner is asking the Applicants to prove their utility statement unequivocally. Thus, the Examiner is applying improperly a standard higher than a preponderance of the evidence standard. In addition, the Examiner has asserted "that the observed overexpression of Grb14 protein in a prostate or breast cell line cannot be unequivocally indicative of Grb14 being a marker for these types of cancer...." September 15, 2005 Office Action at pages 7-8 (emphasis added). This is further evidence that she is employing a standard higher than a preponderance of the evidence standard. Applicants are not required to prove their utility unequivocally.

The burden is on the Office to substantiate any reasons for doubting an asserted utility. The Examiner has cited only a general paper by Baguley *et al.*; in so doing, once again the Examiner has not met the evidentiary standard of a preponderance of the evidence. The Daly *et al.* paper (J. Biol. Chem. (1996) 271:12502-12510) cited previously by Applicant is far more relevant to breast and prostate cancer than is the general Baguley *et al.* paper. Therefore, at best there is a 50-50 tie, Applicants' word against the Examiner's, and a tie is broken in favor of Applicants.

After discussing *Fisher* in the Final Office Action, the Examiner made an unsupported statement that "detection of an isolated polynucleotide molecule of SEQ ID NO:1 or the encoded polypeptide of SEQ ID NO: 2 provides no information regarding presence or absence of any pathological condition, including breast or other form of cancer." First, such a statement does not break the 50-50 tie; it is but another example of the Examiner's unsupported opinion, which is contrary to the evidence of record. Second, the statement is not relevant to all three of Applicants' utilities delineated above. Applicants reiterate that to satisfy the utility requirement an applicant need only provide one credible assertion of specific and substantial utility for each claimed invention. MPEP § 2107.

Applicants submit that *Fisher* is not on point in one respect because the case dealt with ESTs. The court in *Fisher* held that "the claimed ESTs are, in words of the Supreme Court, mere 'object[s] of use-testing,' to wit, objects upon which scientific research could be performed with no assurance that anything useful will be discovered in the end." *Fisher* at 1373 (citation omitted). Unlike in *Fisher*, Applicants' utility statement is supported by evidence which would lead one of ordinary skill in the art to consider Applicants' utility statement credible as well as specific and substantial. However, to the extent that the *Fisher* court stated that the utility threshold is not high (both the applicant and the solicitor agreed to this), it is very much on point. *Fisher* at 1370.

Withdrawal of this rejection is respectfully requested.

Procedural Flaws in the Rejection

The Examiner rejected the claims under 35 U.S.C. § 101 "because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility...." It is unclear from this statement whether the Examiner considers Applicants' utilities 1) credible but not specific and substantial or 2) specific and substantial but not credible. Applicants have requested clarification, but the statement of rejection remains unclear.

The phrasing of the rejection is contrary to the Utility Guidelines, contrary to the MPEP at § 2107 II(C), and even contrary to *In re Fisher*, *supra*, cited by the Examiner. In *Fisher*, the government contended "that a patent applicant need disclose only a single specific and substantial utility ... the very standard articulated in the PTO's 'Utility Examination Guidelines' ... and followed here when examining the ... application." *Fisher* at 1370. It should be noted that the court did not say single specific and substantial credible utility. Based on the court's language, it is apparent that the court and PTO considered Fisher's utility credible, but not specific and substantial. The phrasing of the present

rejection does not allow one to understand (as in *Fisher*) if the utility is considered credible, but not specific and substantial.

The Examiner cited MPEP § 2107 II(B) in response to Applicants request for clarification, but MPEP §2107 II(C) would appear to control, since this latter section discusses how to make the rejection. Applicants again request clarification of the rejection.

Rejection of Claims 5-7, 19-22, 24-29, and 31-41 under 35 U.S.C. § 112, First Paragraph

Review of this rejection is requested.

In summary, the claims were rejected for lacking enablement ("how to use") because the claimed invention is allegedly not supported by either a clear asserted utility or a well established utility for reasons set forth in the rejection under 35 U.S.C. § 101.

Applicants reiterate their arguments above. Because the § 101 rejection is flawed for the reasons set forth above, this rejection must fall. Withdrawal of this rejection is respectfully requested.